

**REMARKS**

Reconsideration is requested.

The claims have been amended to advance prosecution and without prejudice. Entry of the present Amendment is requested. The cells of amended claim 22 are described at page 39, line 15 of the specification. No new matter has been added.

Claims 22, 24, 26, 27 and 29-32 are pending.

The Section 103 rejection of claims 22, 24, 26, 27 and 29-32 over Bellamy (Cancer Research 1999 February, 59:728-733), Shitara (U.S. Patent No. 6,617,160), Rockwell (U.S. Patent No. 5,840,301), and Greenwood et al (Protein Engineering of Antibody Molecules for Prophylactic and Therapeutic Applications in Man, 1993, pp 85-100), is traversed. Reconsideration and withdrawal of the rejection is requested in view of the following distinguishing comments, as well as the attached Declaration of Dr. Shitara.

The presently claimed invention relates to a method for treating leukemia which comprises administering to a leukemia patient a humanized anti-human VEGF Flt-1 antibody having antibody-dependent cellular cytotoxicity (ADCC) activity against leukemia cells which is equal to or greater than that of the humanized anti-human VEGF receptor Flt-1 antibody generated by YB2/3HL.P2.G11.16Ag.20 cells. According to the attached Shitara Declaration, a humanized anti-Flt-1 antibody produced by using a CHO cell line does not have ADCC activity against a leukemia cell line and can not destroy leukemia cells, even if it is a humanized anti-Flt-1 IgG1 antibody prepared in the same manner as in the method of the present specification. On the other hand, according to the previously-submitted Declaration of Dr. Shitara, a humanized anti-Flt-1 antibody

KM2550 (WO99/60026) produced by using YB2/3HL.P2.G11.16Ag.20 cells has significant ADCC activity against a leukemia cell line depending on the antibody concentration. Accordingly, the applicants believe that one of ordinary skill in the art would not have expected such effect that leukemia cells can be destroyed by using a humanized anti-Flt-1 antibody of ADCC activity which is equal or greater than that of the humanized anti-human VEGF receptor Flt-1 antibody generated by YB2/3HL.P2.G11.16Ag.20 cells. The claimed invention therefore is submitted to be patentable over the combination of cited references.

Withdrawal of the Section 103 rejection and a Notice of Allowance are requested.

The Examiner is requested to contact the undersigned in the event anything further is required.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

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